

**Translation**

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PCT/JP2003/015535

PATENT COOPERATION TREATY



**PCT**

**INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY**  
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 3125WO0P	<b>FOR FURTHER ACTION</b>		See Form PCT/IPEA/416
International application No. PCT/JP2003/015535	International filing date (day/month/year) 04 December 2003 (04.12.2003)	Priority date (day/month/year) 05 December 2002 (05.12.2002)	
International Patent Classification (IPC) or national classification and IPC C07D 279/08, A61K 31/5415, A61P 9/00, 13/12, 19/00, 25/00, 29/00, 31/00, 35/00, 37/00, 43/00			
Applicant  TAKEDA CHEMICAL INDUSTRIES, LTD.			

<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>8</u> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>	
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the report</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input checked="" type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input checked="" type="checkbox"/> Box No. VIII Certain observations on the international application</p>	

Date of submission of the demand  08 January 2004 (08.01.2004)	Date of completion of this report  18 June 2004 (18.06.2004)
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/JP2003/015535

## Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

- ☐ This report is based on translations from the original language into the following language \_\_\_\_\_, which is language of a translation furnished for the purpose of:
- ☐ international search (under Rules 12.3 and 23.1(b))
  - ☐ publication of the international application (under Rule 12.4)
  - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☒ The international application as originally filed/furnished

☐ the description:

pages \_\_\_\_\_, as originally filed/furnished

pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_

pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_

☐ the claims:

pages \_\_\_\_\_, as originally filed/furnished

pages\* \_\_\_\_\_, as amended (together with any statement) under Article 19

pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_

pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_

☐ the drawings:

pages \_\_\_\_\_, as originally filed/furnished

pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_

pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_

☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages \_\_\_\_\_

☐ the claims, Nos. \_\_\_\_\_

☐ the drawings, sheets/figs \_\_\_\_\_

☐ the sequence listing (*specify*): \_\_\_\_\_

☐ any table(s) related to sequence listing (*specify*): \_\_\_\_\_

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages \_\_\_\_\_

☐ the claims, Nos. \_\_\_\_\_

☐ the drawings, sheets/figs \_\_\_\_\_

☐ the sequence listing (*specify*): \_\_\_\_\_

☐ any table(s) related to sequence listing (*specify*): \_\_\_\_\_

\* If item 4 applies, some or all of those sheets may be marked "superseded."

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 10, 18

because:

☒ the said international application, or the said claim No. 18  
relates to the following subject matter which does not require an international preliminary examination (*specify*):

The invention of claim 18 concerns a method for treating the human body by therapy.

☒ the description, claims or drawings (*indicate particular elements below*) or said claim No. 10  
is so unclear that no meaningful opinion could be formed (*specify*):

It is unclear which compounds are specifically included in the term "prodrug" among the compounds of claim 1.

☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 10, 18.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐

has not been furnished

☐

does not comply with the standard

the computer readable form

☐

has not been furnished

☐

does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ see Supplemental Box for further details.

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

## 1. Statement

Novelty (N)	Claims		YES
	Claims	1-9, 11-17, 19	NO
Inventive step (IS)	Claims		YES
	Claims	1-9, 11-17, 19	NO
Industrial applicability (IA)	Claims	1-9, 11-17, 19	YES
	Claims		NO

## 2. Citations and explanations (Rule 70.7)

Document 1 [WO 02/18356 A1 (Takeda Chemical Industries, Ltd.) March 7, 2002]

states that 4H-1,3-benzothiazin-4-one having at the 2 position "an optionally substituted hydrocarbon, optionally substituted aromatic heterocyclic group or optionally substituted amino group" (a compound that overlaps with the compounds represented by the general formulas of the claims of this international application) has the effect of inhibiting apoptosis in myocardial cells, and thereby this compound has a preventative and therapeutic effect on heart disease.

Document 2 [WO 02/44157 A2 (ICONIX PHARMACEUTICALS INC.) June 6, 2002]

states that a compound that overlaps with the compounds represented by the general formulas of the claims of this international application (compounds in the general formulas wherein R<sup>2</sup> specifically represents -CH<sub>2</sub>-CONH<sub>2</sub>) has PARP inhibitory activity.

Document 3 [JP 3-229241 A (Fuji Photo Film Co., Ltd.) October 11, 1991]

describes a 4H-1,3-benzothiazin-4-one having at the 2 position "an optionally substituted alkyl group or aryl group" (a compound that overlaps with the compounds represented by the general formulas of the claims of this international application).

Document 4 [US 3470168 A (American Home Products Corporation) September 30, 1969]

describes a 4H-1,3-benzothiazin-4-one having at the 2 position various "amino groups."

Document 5 [GADE, T., et al. "Electroreduction of organic compounds. 19. Formation of benzoanellated sulfur heterocycles by intramolecular cathodic cyclization of dithiocarboxylic esters," *Chemisch Berichte* (1992), 125(1), 127-41]

describes a 4H-1,3-benzothiazin-4-one having at the 2 position a t-butyl group.

## Box No. VI Certain documents cited

## 1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO 03/90782 A1 (Takeda Chemical Industries, Ltd.) EX	03.11.2003	24.01.2003	26.04.2002
WO 03/20719 A1 (Takeda Chemical Industries, Ltd.) EX	13.03.2003	02.09.2002	03.09.2001

## 2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure (day/month/year)	Date of written disclosure referring to non-written disclosure (day/month/year)

**INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY**

International application No.

**PCT/JP03/15535**

**Box No. VIII Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The term "prodrug" is used in the claims, but it is unclear which compounds are encompassed within the scope of that term.

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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## Supplemental Box Relating to Sequence Listing

## Continuation of Box No. 1, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis that of:
- a. type of material
    - ☒ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material
    - ☒ in written format
    - ☒ in computer readable form
  - c. time of filing/furnishing
    - ☒ contained in the international application as filed
    - ☒ filed together with the international application in computer readable form
    - ☐ furnished subsequently to this Authority for the purpose of search and/or examination
    - ☐ received by this Authority as an amendment\* on \_\_\_\_\_
2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

\* If item 4 in Box No. 1 applies, the listing and /or table(s) related thereto, which form part of the basis of the report, may be marked "superseded".

## Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of Box V:

Document 6 [WO 99/11649 A2 (GUILFORD PHARMACEUTICALS INC.) March 11, 1999] states that PARP inhibitors have a protective effect in heart disease. (see "Field of the Invention").

\*Claims 1-8

The inventions of claims 1-8 lack novelty and an inventive step with respect to documents 1-3 and 5 cited in the international search report.

Documents 1-3 and 5 describe compounds that overlap with the compounds of the general formulas of this application.

\*Claims 9, 11-17, and 19

The inventions of claims 9, 11-17 and 19 lack novelty and an inventive step with respect to documents 1, 2, and 6 cited in the international search report.

Document 1 does not state that the compounds represented by the general formulas in the claims of this international application function as "an agent that binds microphage migration inhibitory factor." However, in light of the fact that this international application asserts an effect on heart disease such as inhibition of myocardial cell death, document 1 does disclose that this compound has an inhibitory effect on heart disease. This being the case, this examination finds that there is no essential difference between the inventions of this international application and the invention described in document 1.

Document 2 also does not state that the compounds represented by the general formulas in the claims of this international application function as "an agent that binds microphage migration inhibitory factor." However, it is clear from document 6 that the inhibition of heart disease is brought about by the inhibitory effect on PARP activity described in document 2, and likewise this examination finds that there is no essential difference between the inventions of this international application and the invention described in document 2.